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Seasonal variation of *Pneumocystis jirovecii* infection: analysis of underlying climatic factors

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Abstract

Pneumocystis jirovecii causes severe pneumonia (PCP) in immunocompromised patients. Seasonal changes of PCP incidence may be associated with climate changes. In this first study using multiple linear regression statistics to assess monthly climatic data and *Pneumocystis*, PCP incidence was positively correlated with mean temperature, but not with rainfall or wind strength.

Keywords: Climate, environment and public health, epidemiology, incidence, infection, meteorological factors, *Pneumocystis jirovecii*, *Pneumocystis* pneumonia

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Pneumocystis jirovecii pneumonia (PCP) is one of the most frequent and serious opportunistic infections. However, the modes of transmission of PCP remain unknown. Air-borne

transmission from infected or colonized humans is the favoured model, and environmental sources are also considered [1].

Between January 1989 and December 2006, 757 PCP patients with pneumonia due to *P. jirovecii* were microscopically diagnosed, using mainly bronchoalveolar lavage specimens at the Max-von-Pettenkofer-Institute, which serves the major infectious disease hospitals in Munich (1.3 million inhabitants). In order to analyse climatic effects on PCP incidence, climate data concerning Munich [mean temperature (TMM), total precipitation representing rainfall activity (RSS), mean wind force (FMM), maximum wind-speed (FXX)] were obtained monthly from the German National Meteorological Service (<http://www.dwd.de>). In order to analyse seasonal effects, four groups (variables) were created: summer (May–August), winter (November–February), spring (March–April) and autumn (September–October) according to average monthly TMM.

Since climate data were available only for May 1992 to December 2006, the 576 PCP patients (77.4% HIV-positive) diagnosed during this period were included in a study of the influence of climatic factors on PCP incidence. Analysis took into consideration the pre- and post-HAART years (before and after January 1997).

The pre-HAART mean annual PCP incidence was nearly twice that of the post-HAART period (57.6 vs. 29.6). In May and August PCP incidence was highest (Fig. 1). Bivariate graphical exploration and regression modelling of the influence of weather parameters on monthly incidence rates as dependent variables, with adjustment for mean annual incidence and logarithmic transformation to achieve normal distribution, were performed [SPSS version 12.0 (SPSS Inc, Chicago, IL, USA), STATA 10.0 (StataCorp LP, College Station, TX, USA)]. Results of the linear regression modelling are summarized in Table 1. Fractional polynomial analysis did

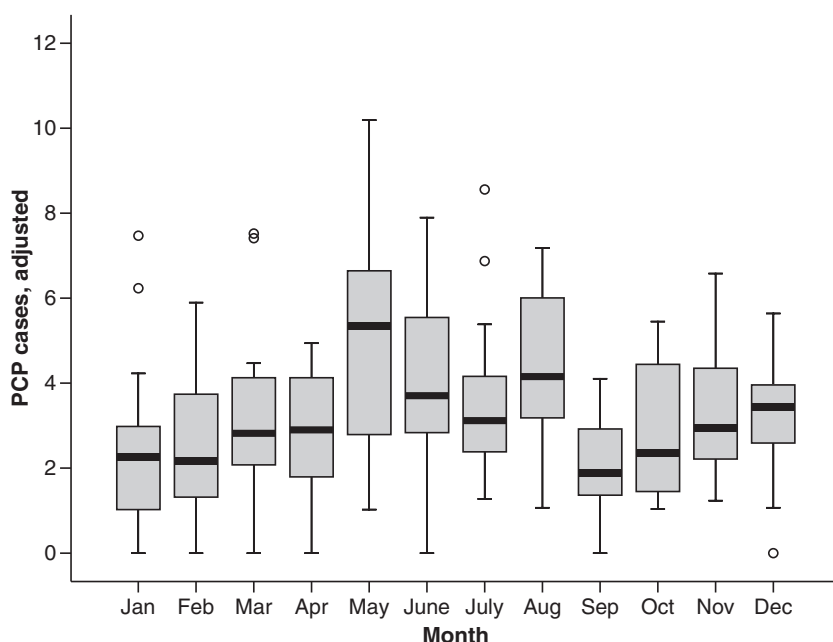


FIG. 1. PCP cases per month, on average (Munich, May 1992 to December 2006). Monthly PCP case numbers were adjusted for annual case numbers (adjustment factor: annual cases/average annual cases).

TABLE 1. Association of climatic factors with monthly PCP case numbers (Munich, May 1992 to December 2006)

Variable	Bivariate				Multiple			
	Coeff. β	95% CI	p	R ²	Coeff. β	95% CI	p	R ²
TMM	0.016	0.005–0.026	0.004	0.048	–0.005	–0.023–0.012	0.551	–
RSS	0.001	–0.001–0.003	0.215	0.009	–0.001	–0.003–0.002	0.641	–
FMM	–0.161	–0.389–0.067	0.166	0.011	0.062	–0.349–0.225	0.671	0.119
FXX	0.001	–0.014–0.017	0.862	<0.001	0.004	–0.014–0.023	0.665	–
HAART	–0.143	–0.309–0.023	0.090	0.016	–0.130	–0.291–0.030	0.111	–
Summer	0.347	0.191–0.503	<0.001	0.099	0.415	0.154–0.676	0.002	–

Bivariate and multiple linear regression models [dependent variable: logarithmic (ln) transformation of adjusted monthly cases + 1; bold: final model].

Variables: mean temperature 2 m above ground (TMM), total precipitation as a measurement for rainfall activity (RSS), mean wind-force (FMM); maximum wind speed at a altitude of 10 m (strongest gust) (FXX); post-HAART vs. pre-HAART (HAART); months May through August (summer).

not improve the model fit [2]. Although no significant correlation was found between PCP incidence and RSS, FMM or FXX, PCP incidence was positively correlated with TMM. Interestingly, the power of the variable 'summer' was much stronger than TMM in explaining PCP incidence. Additional inclusion of any single of the four weather parameters into the model did not have a robust effect on PCP incidence when compared with the variable 'summer' alone. Whereas PCP monthly incidence was independent of the pre- and post-HAART periods, the 'summer' effect was significantly more pronounced in the post-HAART period. Lag modelling considering a 4- or 8-week incubation period, based on animal and human outbreak studies [3–6], had no additional benefit in explaining PCP seasonality.

In contrast to mainly descriptive studies from Spain [7,8] and the UK [9], which showed PCP incidence to be maximal in the winter months, similar to the situation with other infectious respiratory diseases, this first study using multiple linear regression statistics to assess monthly climatic data and PCP incidence has revealed an opposite pattern, with PCP incidence being maximal in the summer months. Moreover, PCP incidence was positively correlated with the mean temperature, but not with rainfall activity or wind strength.

Most previous studies analysing seasonal variations in PCP incidence are mainly descriptive. A seasonal distribution with the highest PCP incidence in winter was observed in the first post-HAART study analysing 498 PCP patients from southern Spain within two consecutive years [7]. These findings were corroborated in another study from southern Spain analysing 536 PCP patients, from both the pre- and post-HAART eras [8]. A similar pattern in 792 patients, with highest PCP incidence in winter and spring, and the most pronounced peak in January, was reported from London between 1985 and 2000 [9]. Strikingly, this seasonal pattern is opposite to that seen in two other London-based studies [10,11]. A more heterogeneous incidence pattern was described in three pre-HAART studies from the USA, the UK and Switzerland, showing PCP peaks in the period March–June (Baltimore, Chicago, Los Angeles, Pittsburgh, 202 AIDS patients [12]), early summer (London, 137 HIV patients [10]) or summer and autumn (Geneva, 93 HIV patients [13]).

In contrast to these descriptive studies, no seasonal clustering of PCP episodes was found in 118 HIV patients from Ohio, USA during the period 1986–1989 [14].

In two of these studies, which additionally reported mean temperature and/or rainfall activity on a purely descriptive level, no clear association between climate factors and PCP incidence could be identified [10,13], while Lubis *et al.* [9] found the lowest rainfall activity in the month with the highest PCP incidence. So far, only one study has explored the

relationship between PCP incidence and climatic factors using statistical methods, reporting an inverse correlation between PCP incidence and the mean temperature for southern Spain, but without influence of relative humidity on the number of PCP patients [8].

In comparison with these previous studies, the current study is based on a statistically more comprehensive and powerful methodology, using four different climatic factors as variables that may influence PCP incidence. In contrast to the studies from the UK and Spain, a clear positive correlation was found between PCP incidence and the mean monthly temperature, whereas rainfall and wind strength were not found to be correlated with PCP incidence. Therefore, these results do not support the concept of increased incidence of *Pneumocystis* infection during colder months, as is the case with other respiratory pathogens [8]. Also, the idea that prior upper respiratory infections might increase susceptibility to *P. jirovecii* [7,12] is not supported by our time lag analysis.

Strikingly, the influence of temperature on PCP incidence was by far exceeded by the seasonal effect of the variable 'summer' (TMM 14.2 ± 1.2 – 18.6 ± 1.7). A possible explanation for the stronger influence of season, compared with that of single climate parameters, might be that season-dependent factors besides climate, such as human behaviour or type of leisure activity, might be relevant for *Pneumocystis* transmission.

In conclusion, this study and others indicate that seasonal variations in PCP incidence exist, albeit to different extents and with different tendencies. Among the analysed climatic parameters, TMM is the most strongly correlated factor—again to different extents and with different tendencies. However, other factors may better explain seasonal variations in PCP incidence. The controversial data from two London-based studies [9,10], i.e. the clustering of different *P. jirovecii* genotypes according to patients' locale in London [11,15], and the presence or absence of an association between certain *P. jirovecii* genotypes and climatic factors [16], suggest that local parameters may also be important.

Transparency Declaration

The authors declare the absence of financial support and no conflict of interest.

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